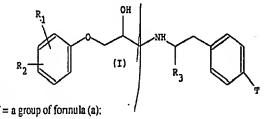
YAMANOUCHI PHARM CO LTD *JP 10007647-A

96.06.25 96JP-164233 (98.01.13) C07C 335/20, A61K 31/17, 31/24, C07D 317/58, A61K 31/275, 31/36

New thiourea derivatives - are beta-3 receptor agonists which accelerate insulin secretion and elevate insulin sensitivity, useful for treating diabetes

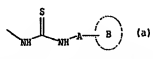
C98-041612

Thiourea derivatives of formula (I) and their salts are new.



T = a group of formula (a):

B(10-A13B, 14-S4) .2



R_1, R_2 = H, halo, hydroxyl, cyano, nitro, trifluoromethyl, lower alkoxyl, lower acylamino, lower alkylsulphonylamino, lower alkoxycarbonylamino, N'-lower alkylureido or lower alkyl (optionally substituted);

R_3 = H or lower alkyl;

A = a bond, lower alkylene or lower alkenylene; and

ring B = optionally substituted aryl or cycloalkyl.

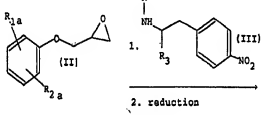
USE

(I) are β-3 receptor agonists and are useful for treating diabetes. (I) accelerate insulin secretion and elevate insulin sensitivity.

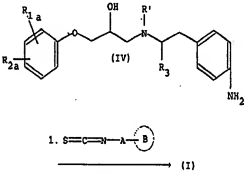
JP 10007647-A+

PREPARATION

E.g.



2. reduction



2. deprotect

R_{1a}, R_{2a} = protecting group for R_1, R_2 and OH; and

R' = amino protecting group.

EXAMPLE

(S)-1-[4-[2-[N-t-Butoxycarbonyl-N-(2-hydroxy-3-

JP 10007647-A+/1

98-126135/12

phenoxypropyl]amino]ethyl]phenyl]-3-phenylthiourea (0.33 g) dissolved in methanol (10 ml) and 4 N hydrogen chloride ethyl acetate solution (10 ml) were mixed and stirred at room temperature for 1 hour to give 0.17 g (S)-1-[4-[2-[(2-hydroxy-3-phenoxypropyl]amino]ethyl]phenyl]-3-phenylthiourea (Ia).HCl, m.pt. 214-217 °C. (MHG)

(20pp002DwgNo.0/0)

JP 10007647-A/2